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Chair and Department of Internal Medicine, Medical University of Lublin

WOJCIECH BARUD, STANISŁAW OSTROWSKI, ROBERT PALUSIŃSKI

Effect of 3-month dihydrotestosterone (DHT) treatment on respiratory function in males with coronary artery disease

Normal male aging is accompanied by a decline in testosterone level and this phenomenon may be accompanied by deterioration of many physiological functions including sexual dysfunction, loss of muscle and bone mass associated with an increase in adiposity and decreased general well being. Clinical studies indicate that some of these clinical sympoms are relieved by replacement therapy. Testosterone substitution can improve sexual function and the quality of life, muscle strength and bone mass. Low testosterone levels appear to be accompanied by an increased cardiovascular risk. Some studies sugest reduction of myocardial ischemia as a result of androgen treatment (1).

Dihydrotestosterone (DHT), natural potent, selective androgen, is formed through 5α-reduction of testosterone by the enzyme 5α-reductase. It has a higher affinity to androgen receptor than testosterone and cannot be aromatized to estrogens.

The aim of this study was to evaluate the effects of three months' DHT treatment on the function of the respiratory system in aging males with coronary artery disease.

MATERIAL AND METHODS

A group of 11 males at the mean age of 58.5±5.4 years with a history of myocardial infarction, but no evidence of obstructive pulmonary disease and prostate cancer was included in this study. Each patient was asked to apply every evening 2 doses (32 mg) DHT on the skin of the abdomen for 3 months. DHT in the form of 0.7% hydroalcoholic gel for transdermal use, was a kind gift from Besins Iscovesco (Paris, France). The placebo group comprised 8 patients at the mean age of 58.1±8.8 years.

Before the treatment and after its cessation each subject had body pletysmography, with the assessment of airway resistance, static lung volumes and parameters of forced expiration. Lung function was performed with Master Screen body box (Jaeger, Germany) according to ATS criteria (2).

The study protocol was approved by the Medical University Board for Supervising Ethics in Medical Experiments and written informed consent was obtained from each person before enrollment. Results are expressed as Mean ± SD. Statistical analysis was performed using Statistica 6.5 for Windows. Student's paired t test was used to compare measurements in the same group before and after treatment. P value <0.05 was considered statistically significant.

RESULTS

The results of respiratory function examination in the DHT and Placebo group are shown in Table 1. DHT treatment was associated with significant increase of peak expiratory flow (PEF) from 8.21±1.71 l/s to 9.19±1.50 l/s (p=0.0019). No significant changes of forced expiratory volume in 1 sec (FEV_1), forced vital capacity (FVC), Tiffenau ratio (FEV_1/FVC), flow-volume (FEF_{25}, FEF_{50}, FEF_{75}), airway resistance (Rt), residual volume (RV) and total lung capacity (TLC)

were observed. The effects of DHT treatment on sex hormones, lipid profil, insulin resistance, fibrinogen and myocardial ischemia have been reported previously (3, 4).

Table 1. Respiratory function parameters in DHT and placebo treated group (Mean ± SD)

	DHT			Placebo		
	before	after	P	before	after	P
PEF (l/s)	8.00 ± 1.57	9.19 ± 1.50	0.0019	6.97 ± 2.39	7.01 ± 1.61	0.95
FEF_{25} (l/s)	7.38 ± 2.15	7.70 ± 2.19	0.51	6.02 ± 1.61	5.92 ± 1.83	0.12
FEF_{50} (l/s)	3.91 ± 1.92	3.65 ± 1.57	0.31	3.53 ± 2.27	3.20 ± 1.57	0.51
FEF_{75} (l/s)	1.01 ± 0.61	0.92 ± 0.48	0.52	1.01 ± 0.69	0.77 ± 0.48	0.18
FVC (l)	4.27 ± 0.71	4.20 ± 0.62	0.47	3.91 ± 0.64	3.96 ± 0.49	0.71
TGV (l)	3.29 ± 0.46	3.38 ± 0.50	0.24	3.61 ± 0.68	3.16 ± 0.93	0.08
RV (l)	2.16 ± 0.31	2.26 ± 0.55	0.49	2.51 ± 0.41	2.43 ± 0.32	0.26
TLC (l)	6.43 ± 0.78	6.54 ± 0.64	0.59	6.51 ± 0.85	6.34 ± 0.92	0.14
FEV_1 (l)	3.36 ± 0.74	3.26 ± 0.64	0.27	2.99 ± 0.64	3.00 ± 0.45	0.94
Raw (kPa/l/s)	0.28 ± 0.16	0.25 ± 0.10	0.24	0.30 ± 0.09	0.27 ± 0.11	0.81
FEV_1/FVC (%)	78.2 ± 8.8	77.7 ± 7.2	0.72	76.3 ± 10.8	76.0 ± 8.8	0.83

DISCUSSION

It has been reported that androgen replacement in aging hypogonadal males improves the sense of well-being and libido, increases muscle mass and strength, improves stamina, preserves or improves bone mass and prevents fractures (14). Some data suggest that androgen supplementation in men with coronary artery disease reduces chest pain and myocardial ischemia in objective responses to cardiac stress testing (3, 6).

Despite increasing androgen use in aging males, few studies have examined breathing and lung function during replacement therapy (9). Some of them suggest unfavourable relationship between testosterone and breathing because androgen treatment can exacerbate the sleep apnea syndrome (11). It is more likely that high, supraphysiological rather than low doses of testosterone worsen sleep and breathing. Moreover, that study has not shown any concomitant changes in upper airway dimensions suggesting that the effect of testosterone on breathing is due to influence on the central respiratory controller (10).

Similarly, little research has examined the relationship between hormone replacement therapy and pulmonary function in postmenopausal women. Estrogen and progestagen substitution was hypothesized to be associated with higher FEV_1, higher FVC and less pulmonary obstruction (5).

The aim of our study was to assess the influence of DHT therapy on respiratory function in older males with coronary artery disease. DHT is the product of conversion from testosterone through the 5α-reductase enzymes and binds to androgen receptor more avidly than testosterone. DHT is a selective, nonaromatizable androgen and its mechanisms of action could not be explained by androgen conversion to estrogen. As a result of 3-month, transdermal DHT therapy there was a significant increase of peak expiratory flow (PEF). The other flow-volume indices remain unchanged. This peak flow improvement in older men in our study seems to be most likely a result of increased muscle strenght than of reduced contractility or increased relaxation of the bronchial muscle. Several plausible mechanisms for a beneficial effect of androgens on muscle strength have been postulated: these include increased muscle protein synthesis, decreased muscle protein degradation and induction hypertrophy of skeletal muscle fibers (8). Anabolic effects of androgens on muscle may be mediated by the antiglucocortycoid action of androgens. Animal study has shown that concomitant administration of androgens with corticosteroids blunted the impact of corticosteroids on respiratory muscle function (7). Oxandrolon therapy (20 mg/d) in

tetraplegic patients produced significant improvement in respiratory parameters (12). In case of oxandrolone androgens increase muscle mass and strength by increasing androgen receptor expression in the skeletal muscle.

As expected, the mean values of FEV_1, FVC, Tiffenau ratio (FEV_1/FVC), RV, TLC and Rt did not change with DHT treatment. Androgen treatment seems not to influence airway dimensions. The previous study on men with chronic obstructive pulmonary disease treated with testosterone (250 mg of testosterone every fourth week during the 26 weeks' study period) has not shown any improvement in pulmonary function (13). Our findings indicate that short 3-month DHT treatment influences only peak expiratory flow (PEF). It may suggest that androgens affect pulmonary function rather by increasing muscle strength than by reducing airway obstruction or restriction of total lung capacity. These findings emphasize the need for further research into the influence of androgens on ventilatory function.

CONCLUSIONS

DHT treatment is associated with improvement of peak expiratory flow (PEF) which may be related to increased muscle strength in the studied males. DHT treatment does not affect airway resistance, or static and dynamic lung volumes.

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SUMMARY

Clinical studies indicate beneficial effects of androgens in aging males with hypogonadism, such as the improvement in sexual function and the quality of life, muscle strength and bone mass. The aim of the study was to assess the effect of 3-month treatment with dihydrotestosterone (DHT) on the function of the respiratory system. The group of 11 males at the mean age of 58.5 ± 5.4 years with a history of myocardial infarction, but no evidence of obstructive pulmonary disease and prostate cancer were treated with transdermal form of DHT (0.7% gel) 32 mg bid for 3 months. Before the treatment and after its cessation each subject had body pletysmography, with the assessment of airway resistance, static lung volumes, and parameters of forced expiration. Three-month DHT treatment was associated with significant increase of peak expiratory flow (PEF) from 8.21±1.71 l/s to 9.19±1.50 l/s (p=0.0019). No significant changes of forced expiratory flow in 1 sec (FEV_1), forced vital capacity (FVC), Tiffenau ratio (FEV_1/FVC), flow-volume (FEF_{25}, FEF_{50}, FEF_{75}), airway resistance, residual volume (RV) and total lung capacity (TLC) were observed. Peak expiratory flow (PEF) improvement associated with DHT treatment may be related to increased muscle strength in the studied males. DHT does not affect airway resistance, or static and dynamic lung volumes.

Wpływ trzymiesięcznego leczenia dihydrotestosteronem na czynność układu oddechowego u mężczyzn z chorobą wieńcową

Badania kliniczne przemawiają za korzystnym działaniem androgenów u starszych mężczyzn z hipogonadyzmem, w tym na poprawę funkcji seksualnych i jakość życia, siłę mięśni, masę kości. Celem pracy była ocena wpływu trzymiesięcznego leczenia dihydrotestosteronem (DHT) na czynność układu oddechowego. U 11 mężczyzn w wieku 58,5±5,4 lat po przebytym zawale mięśnia serca, u których wykluczono obturacyjną chorobę płuc i nie stwierdzano raka gruczołu krokowego, stosowano przezskórnie DHT (2 dawki) w formie 0,7% żelu (32 mg) przez okres trzech miesięcy. Przed leczeniem i po jego zakończeniu mierzono opór dróg oddechowych, statyczne objętości płuc oraz parametry natężonego wydechu z pomocą pletyzmografu kabinowego. W wyniku trzymiesięcznego stosowania DHT nastąpił istotny wzrost szczytowego przepływu wydechowego (PEF) z 8,21±1,71 l/s do 9,19±1,50 l/s (p=0,0019). Nie stwierdzono istotnych zmian natężonej objętości wydechowej 1-sek (FEV_1), natężonej objętości życiowej (FVC), wskaźnika Tiffenau (FEV_1/FVC), natężonego przepływu wydechowego (FEF_{25}, FEF_{50}, FEF_{75}), oporu dróg oddechowych (Rt), objętości zalegającej (RV) i całkowitej pojemności płuc (TLC). Stosowanie DHT w istotny sposób wpłynęło na poprawę wskaźnika szczytowego przepływu wydechowego, co może być wynikiem zwiększenia siły mięśniowej u badanych mężczyzn. Stosowanie DHT nie wpływało na opór dróg oddechowych oraz statyczne i dynamiczne objętości płuc.